

DETAILED DESCRIPTION OF THE PREFERRED EMBODIMENTS

With reference to Figures 1-4, it was found that 50% inhibition in renal uptake of [<sup>111</sup>In-DTPA-D-Phe<sup>1</sup>]octreotide in rats could be achieved by D-Lysine or L-lysine at 400 mg/kg. L-arginine alone gave a reduction of 20-30% at an equimolar dose. In human studies 15, 21 and 40% reduction of kidney uptake of [<sup>111</sup>In-DTPA-D-Phe<sup>1</sup>]octreotide was reached using a dose of 25, 50 and 75 g L-lysine, respectively. The doses of 25 and 50 g L-lysine were well tolerated without any toxicity noted, but the 75 g L-lysine dose was associated with severe hyperkalemia in 50% of the patients. Hyperkalemia may result in acute and life-threatening cardiotoxicity.

**Please delete the specification paragraph beginning at page 4, line 25.**

IN THE CLAIMS:

**Please cancel original claims 1-20 and rewrite them as new claims 21-52 as follows:**

21. A method for the preparation of a composition for inhibiting renal uptake of substances, in particular proteins or peptides, that may be damaging to the kidneys and that are used for therapeutical or diagnostic purposes, the method comprising:

providing the combination of a first compound which is lysine, or an amino acid or other proteinaceous moiety having a free amino group with a pKa substantially similar or equal to that of lysine, or pharmaceutically acceptable salts or carboxyl derivatives thereof; and

a second compound, which is a positively charged compound, or pharmaceutically acceptable salts or carboxyl derivatives thereof.

22. The method as claimed in claim 21, wherein the positively charged second molecule is a positively charged amino acid, or pharmaceutically acceptable salts or carboxyl derivatives thereof.

23. The method as claimed in claim 22, wherein the positively charged amino acid is selected from the group consisting of arginine, ornithine and citrulline, or pharmaceutically acceptable salts or carboxyl derivatives thereof.

24. The method as claimed in claim 21, wherein the first compound is lysine selected from D-lysine, L-lysine or poly-lysine.

25. The method as claimed in claim 21, wherein the first compound is lysine and the second compound is arginine.

26. The method as claimed in claim 21, wherein the amount of the first compound is 10-45 grams per treatment.

27. The method as claimed in claim 21, wherein the amount of the first compound is 15-35 grams per treatment.

28. The method as claimed in claim 21, wherein the amount of the first compound is 20-30 grams per treatment.

29. The method as claimed in claim 21, wherein the amount of the first compound is about 25 grams per treatment.

30. The method as claimed in claim 21, wherein the amount of the second compound is 15-45 grams per treatment.

31. The method as claimed in claim 21, wherein the amount of the second compound is 15-35 grams per treatment.

32. The method as claimed in claim 21, wherein the amount of the second compound is 20-30 grams per treatment.

33. The method as claimed in claim 21, wherein the amount of the second compound is about 25 grams per treatment.

34. The method as claimed in claim 21, wherein the first compound is lysine in an amount of about 25 grams and the second compound is arginine in an amount of about 25 grams per treatment.

35. The method as claimed in claim 21, wherein the two compounds are administered in about 1 L infusion fluid over a period of about 4 hours.

36. The method as claimed in claim 21, wherein the substances that may be damaging to the kidneys, and of which the renal tubular uptake is to be inhibited are proteins, peptides or monoclonal antibodies, in particular proteins, peptides or monoclonal antibodies that are inherently toxic, that are coupled to a radionuclide, a cytostatic agent, a toxic agent, a metal, or a combination thereof, or cytostatic agents and nephrotoxic antibiotics per se.

37. A therapeutical composition for the inhibition of the renal uptake of substances, in particular proteins or peptides, that may be damaging to the kidneys and that are used for therapeutical or diagnostic purposes, which composition comprises one or more pharmaceutically acceptable excipients, carriers or diluents and a combination of:

a first compound which is lysine, or an amino acid or other proteinaceous moiety having a free amino group with a pKa substantially similar or equal to that of lysine, or pharmaceutically acceptable salts or carboxyl derivatives thereof; and

a second compound, which is a positively charged compound, or pharmaceutically acceptable salts or carboxyl derivatives thereof.

38. The therapeutical composition as claimed in claim 37, wherein the positively charged second molecule is a positively charged amino acid, or pharmaceutically acceptable salts or carboxyl derivatives thereof.

39. The therapeutical composition as claimed in claim 38, wherein the positively charged amino acid is selected from the group consisting of arginine, ornithine and citrulline, or pharmaceutically acceptable salts or carboxyl derivatives thereof.

40. The therapeutical composition as claimed in claim 37, wherein the first compound is lysine selected from D-lysine, L-lysine or poly-lysine.

41. The therapeutical composition as claimed in claim 37, wherein the first compound is lysine and the second compound is arginine.

42. The therapeutical composition as claimed in claim 37, wherein the amount of the first compound is 10-45 grams per treatment.

43. The therapeutical composition as claimed in claim 37, wherein the amount of the first compound is 15-35 grams per treatment.

44. The therapeutical composition as claimed in claim 37, wherein the amount of the first compound is 20-30 grams per treatment.

45. The therapeutical composition as claimed in claim 37, wherein the amount of the first compound is about 25 grams per treatment.

46. The therapeutical composition as claimed in claim 37, wherein the amount of the second compound is 15-45 grams per treatment.

47. The therapeutical composition as claimed in claim 37, wherein the amount of the second compound is 15-35 grams per treatment.

48 The therapeutical composition as claimed in claim 37, wherein the amount of the second compound is 20-30 grams per treatment.

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49. The therapeutical composition as claimed in claim 37, wherein the amount of the second compound is about 25 grams per treatment.

50. The therapeutical composition as claimed in claim 37, wherein the first compound is lysine in an amount of about 25 grams and the second compound is arginine in an amount of about 25 grams per treatment.

51. The therapeutical composition as claimed in claim 37, wherein the two compounds are present in about 1 L infusion fluid.

52. The method for inhibiting the renal uptake of proteins or peptides, that are used for therapeutical or diagnostic purposes, in a subject, which method consists of the administration of a therapeutical composition as claimed in claim 37.

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**IN THE ABSTRACT:**

After the claims, please insert a page containing the Abstract Of The Disclosure, which is attached hereto as a separately typed page.

**REMARKS**

The specification and claim amendments have been made in order to conform this patent application to customary United States patent practice.

Attached hereto is a marked-up version of the changes made to the specification by the current amendment. The attachment is captioned "VERSION WITH MARKINGS TO SHOW CHANGES MADE".